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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,606	12/27/2001	Hidemitsu Nishida	1110-0306P	9102
2292	7590	03/17/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			PATEL, SUDHAKER B	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/026,606	Applicant(s) NISHIDA ET AL.	
	Examiner Sudhaker B. Patel, D.Sc.Tech.	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-29 is/are pending in the application.
- 4a) Of the above claim(s) 25 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-24 and 27-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 December 2001 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/17/02 & 9/27/02</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicants' communication paper dated 12/30/03 is acknowledged.

Election/Restrictions

Applicant's election with traverse of invention of Group I and species of species of Example 1 in Paper dated 12/30/03 is acknowledged. The traversal is on the ground(s) that specification discloses Example 8 consisting of a tricyclic heterocycle other than invention of Group I with a core: "2,4-diaza-7-oxa-spirobicyclo [4.4.0] decane-2-one, and other compounds as recited in page 93 and others. This is not found persuasive because of the reasons already provided in the earlier communication page 11/20/03. d. Additionally, the basic tricyclic core with X, Y, Z, A, B, D, T, Q components and integers m, n, l consist of multiples of variables, will provide different tricyclic chemical structures which are not art recognized equivalents. e.g. (1). When X involves cyclohexane ring. (2). When X is saturated piperidine ring. (3). When Y is Oxygen, and integers m, n forming a 5-membered ring that is furan. (4). When Y is Oxygen, and m, n forming a 6-membered ring that is pyrane. (5). When Y is Sulfur, and m, n forming a 5-membered ring that is thien. (6). When Y is Sulfur, and m, n forming a 6-membered ring that is thiopyrane. (7). When n is 1, the core is 6-membered 1,4-diaza/piperazine. (8). When n is 2, the core is 7-membered 1,4-diaza, or (1,4)diazepine or their -one forms. Therefore, the compounds of Groups I and II are drawn to:

- (1). Structurally diverse and **patentably distinct species** with a wide variety of compounds that are made and used independently of each other;
- (2). Species/Compounds are separately classified;
- (3). Classes/subclasses will require separate literature searches;
- (4). Species/Compounds are not art recognized equivalents, and additionally,
- (5). The groups lack unity of invention (see MPEP 803.02).

Based on above stated data i.e. (1) - (5), claims also lack unity of invention.

The invention of Group I falls in class 544 with a core as identified and stated earlier in this paper. This core of invention of Group I is different than Example 8 which falls in class 540 according to the U.S. Patent Classification system.

The search for **invention of Group I** according to the U.S. Patent Classification System for class 544, subclasses 358, 380, 384, provided more than 1000 hits; and the search for utility class 514, subclasses 248, 245, 250, 252.15, 252.13 provides 3000 hits.

Examiner has searched invention of Group I related to species of Example 1 only. Some of the species of invention of Group II will fall in class 540, subclasses 543, 547, 553, 557, 569, 570; class 514, subclasses 183, 211.01, 211.03, 211.04, 211.08.

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Preliminary search provided a total hits of more than 1000 for class 540 and more than 2000 hits for its utility class. Note, although the main utility class 514 is the same, the subclasses are different, and for a thorough and complete examination of this application as a single piece, more time will be required. These numbers will increase with search required for rest of the species.

The total hits for elected invention of Group I alone will be more than 4000.

It is this search and examination which is time consuming and burdensome for additional species/compounds which are included in the definition of X, Y, Z, A, B, D, T, Q components and integers m, n, l forming chemically different and patentably distinct species/ compounds.

Applicants are reminded of the election of species guidelines provided in MPEP 803.02, which are followed for the examination.

The elected species of compound of Example 1 as stated earlier has following meanings for variables in the generic Formula (I) of claim 1 forming a tricyclic-spiro compounds of generic formula (I), wherein X is Nitrogen substituted pyridine in the bridge A-B- : Y = oxygen atom group forming a 5-membered furan ring when integer m = zero, integer l = 1, integer n = 1 i.e. 3-fused rings combination as 6-membered saturated piperidine-5-membered (saturated hetero-ring) -6-membered 1,4-diaza-piperazine consisting of; (1). Piperidine-1,4-diaza-7-oxa-spirobicyclo[4.3.0]-nonanone.

Initial search with above definitions of the variables no prior art was found. Therefore, search was expanded to the rest of species of the invention of Group I wherein Y = other than Oxygen (See rejections and allowable subject matter below).

Since claims 19-24, 27-29 link with other inventions, they will be examined bearing in mind the subject matter and species as elected by applicants and restriction as stated above only. Claims 25, 26, and all other definitions than stated above for Y component and integers m, n, l are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected subject matter, there being no allowable generic or linking claim.

Examiner appreciates applicants' IDS papers.

The restriction/election requirement is still deemed proper, is maintained, and is therefore now made FINAL.

First action on merits follows.

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Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 6/17/02 & 9/27/02 are being considered by the examiner. A signed copy of the PTO Form 1449 are enclosed with this communication for applicants' record.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3a. Claims 19-24, 27-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10451728 filed 6/25/2003. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims include compounds and compositions similar to the ref. '728. See compounds of Formula (I) in claim 1 in pages 319-320, claim 2 compounds, claim 7 compounds in pages 322-335, and pharmaceutical composition claim 9 in page 335, lines 15-19.

3b. Instant claims 19-24, 27-29 differ from the above ref. '718 claims by reciting a broader pharmaceutical activity related to the X-ray structure of the same compounds. The compounds of both of the cases are not yet patented, and the method of use(s) as recited are related to the structurally same chemicals/ compounds dependent on their pharmacological activity, which would extend, the monopoly of the instant U.S. Application Sr. No. 10026606, filed 12/27/01.

3. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 19-24,27-29 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply.

6. Claim 19 recites A, Q components as (where applicable) a Hydrogen atom or a Hydrocarbon group or a (un)saturated 5- or 6- membered heterocyclic group or imidoyl group or a heterocyclic group which are optionally substituted. The claim remains silent about the nature, number, and arrangement of heterocyclic atoms and their relation to the point of attachment with the main core bridge(s). Q component's exact hetero rings as recited in the working examples are suggested.

7. Claim 20,27,29 recite "at least" is not acceptable, *Petrolite Corp. v. Watson*, Comr. Pats., 113 USPQ 248. Correction is required.

8. Claim 21 which is dependent on main claim 19 defines Q component as C6-14 aryl which is optionally substituted, and the same is not definitely defined in claim. Thus, Claim 21 recites the limitation of "Q" component of claim 19. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 22 recites, "A pharmaceutical composition characterized by that the composition contains a compound represented by Formula (I) or its pharmaceutically acceptable salt as an effective component". Thus, claim remains silent about the exact make up of the composition. Usually, pharmaceutically acceptable carrier(s) are present in the composition(s). Correction is required.

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10. Claim 23 recites "A FXa inhibitor.... Pharmaceutically acceptable salt as and effective component". Correction to: "A FXa inhibitor.... Pharmaceutically acceptable salt as an therapeutically effective component" is required.
11. Claim 24 recites "-X =". There is only X component in the Formula (I'). X can be -CH- or -N- only and can not have a double bond. Correction(s) is required.
12. Claim 28 recites "administration of the pharmaceutical composition of claim 27 to a mammal which requires inhibition of the FXa". Correction to: "administration of the therapeutically effective amount of the pharmaceutical composition of claim 27 to a mammal which requires inhibition of the FXa" is required.
13. Claim 29 recites "Crystal of a complex....compound or its salt of independent claims 24-26". Claims 24 remains silent about the nature of complex as well crystal. Correction is required.

Conclusion

Allowable Subject Matter

14. Claim 19-24, 27-29 related to the invention of Group I subject matter as elected by the applicants, would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph and other rejections, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.
15. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art ref. Das et al (U.S.P. 5691356, dated 11/1997) teaches disubstituted heterocyclic thrombin inhibitors with a core: "Azacycloalkyl- substituted 5 to 7-membered saturated heterocycle with 1 Nitrogen atom only wherein the N is connected to a bridge -CO-CHR-Z-R4". The ref. '356 does not indicate or suggest to arrive at the instant invention with a core: "A-B-spiro-piperidine: furane-1,4-diazine-T-Q".
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is (571) 272-0671.

The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday).

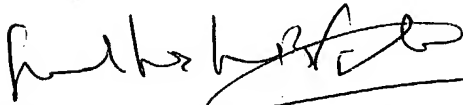
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on (571) 272 0674 or Sr. Examiner Mr. Richard Raymond at (571) 272 0673 or Mr. James Wilson at (571) 272-0661.

The assigned centralized fax number for the organization/USPTO for processing of this application or its proceedings is (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sudhaker B. Patel, D.Sc. Tech.
March 15, 2004.



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ART UNIT 1624